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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/091,166	03/05/2002	David A. Adler	97-44D1	7711

7590 12/02/2004

EXAMINER
BUGAISKY, GABRIELE E

ART UNIT	PAPER NUMBER
1653	

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DATE MAILED: 12/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,166	ADLER ET AL.	
	Examiner	Art Unit	
	Gabriele E. BUGAISKY	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,21-26,28,29,37,38 and 40-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 21-26, 28-29, 37-38, 40-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/5/2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/02.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I in the reply filed on 9/30/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

All pending claims are to the elected invention.; claims 6-7 are not withdrawn, as stated in the election. Rather, they have been cancelled.

Priority

This application repeats a substantial portion of prior Application No. 09/636399, filed 8/10/2000, and adds claims to additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Since the added material in the claims is not supported by the original application as filed, this application cannot be considered a divisional application *per se*. Should Applicants wish to pursue claims directed to subject matter not disclosed in the parent application, filing a CIP may be appropriate, once the description is amended to adequately describe the claimed invention.. Alternatively, amendment to delete the additional new subject matter would permit this application to be properly prosecuted as a divisional application.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see e.g., page 73, lines 33-34). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The use of trademarks such as FICOLL, SEPHAROSE and TOYOPEARL has been noted in this application (e.g., page 36, line 24, page 59, lines 8 and 11, page 59, line 12, respectively). Each should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Each amendment filed 10/15/2002 and 9/2004 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The disclosure of 09/636399, of which this

application is a divisional does not describe the pharmaceutical treatment for the following microorganisms: *Burkholderia cepacia, Stenotrophomonas maltophophilia, Haemophilus influenzae, Staphylococcus aureus, and Aspergillus fumigatus*. Further, the following are described only as potential organisms for screening antimicrobial activity, and are not described in the context of pharmaceutical treatment: *Klebsiella, Mycoplasma*, *Candida albicans,* and *Pseudomonas aeruginosa*. *Escherichia coli* is described as a potential organism for screening antimicrobial activity and as a cloning host, not as a subject for pharmaceutical treatment. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26, 28-29, 37-38, and 40-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants have introduced new matter into the claims which was not disclosed in the filed specification of the parent application (as discussed above). Since the independent and broader claims encompass the specifically recited new subject matter, they must be included in this ejection.

Claims 1-2 , 4, 44, and 47-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for proteins comprising aa 23-65 of either SEQ ID NO:2 or SEQ ID NO: 10, does not reasonably provide enablement for any protein which is at least 95% identical to proteins comprising either SEQ ID NO:2 or SEQ ID NO:10, even if cysteines are maintained as specified in claim 44. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. SEQ ID NO:10 is identical to SEQ ID NO:2 except that it contains two additional lysines at the carboxyl terminus. Applicants have essentially supplied but a single protein and identified the secreted form of the polypeptide. It is stated in the specification that computer modeling has been performed, but information is not presented in such a way that one can readily assess how substitutions at different positions would affect the folding of a mutated protein. Also, no mutants with defensin like properties have been presented. The specification provides no mutants and no guidance as to where the mutations may occur. There is thus no predictability as to which residues may be substituted so that the encoded protein still acts like zamp1

In *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). the issue of enablement in molecular biology was considered. There are eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented;(c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

Although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and retain or achieve the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. The specification does not support the broad scope of the claim which encompasses all substitutions, additions or deletions because while the specification does disclose specific positions and regions throughout the protein's sequence which can be predictably modified, it does not disclose the following : (A) the general tolerance to modification and extent of such tolerance; (B) which regions are critical for biological activity; (C)what fragments, if any, can be made which have the desired biological activity of the intact protein; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Wells discusses that although one may reasonably make single conservative substitutions in a protein, the effect of multiple mutations cannot be well predicted, as often such mutants will not fold correctly. Applicants have provided no mutants, and there is no way to predict where one may profitably make variants which encode homologs that retain defensin activity.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what "corresponding to" is meant to convey. If it is intended that when aligned with SEQ ID NO:2 or 10, the claimed proteins have cysteines in the same position as the reference sequence(s), then the claim should clearly state so.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 50 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 64 of copending Application No. 10/409,366. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 21-26, 28-29, 37-38 and 40-50 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-43 and 45-90 of copending Application No. 10/272121. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the scope of the claims varies, each set includes recited embodiments of the other application. The pharmaceutical compositions of claims 26-43 and 45-90 of '121 comprise the purified isolated proteins that are at least 95% identical to aa 23-67 of SEQ ID NO:10 of the instant application . Claim 26 of the '121 application recites embodiments d) , e), f), g) and j) that are identical to embodiments b)-f) of claim 5 of the instant application . It is deemed obvious to use a pharmaceutical in a pharmaceutical method of use.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-5, 21-26, 28-29, 37-38 and 40-50 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 26-65 of copending Application No. 10/409366. Although the conflicting claims are not identical, they are not patentably distinct from each other because while the scope of the claims varies, each set includes recited embodiments of the other application. The instant polypeptides of claim 1 are encompassed within the claimed subject matter of claim 26 of the '366 application,

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 6809181 (McCray *et al.*) reveals human β-defensin-3, which is identical to zamp1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gabriele E. BUGAISKY whose telephone number is (571) 272-0945. The examiner can normally be reached on Tues.- Fri 8:15 AM-1:45 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gabriele E. BUGAISKY
Primary Examiner
Art Unit 1653

11/23/2004